

CLEAN VERSIONS OF AMENDED SPECIFICATION PARAGRAPHS

The paragraph beginning at line 1, page 10 of the specification is amended to read as follows:

Figure 2. Structural analysis of rAAV circular intermediates in HeLa cells (agarose gel, left; Southern blot, right). Circular rAAV intermediate clones isolated from AV.GFP3ori infected HeLa cells were analyzed by diagnostic restriction digestion with AseI, SphI, and PstI together with Southern blotting against ITR, GFP, and Stuffer ³²P-labeled probes. In panel A, four clones representing the diversity of intermediates found (p190, p333, p280, and p345) gave a diagnostic PstI (P) restriction pattern (3kb and 1.7kb bands) consistent with a circular monomer or multimer intact genome. SphI (S) digestion demonstrated existence of a single ITR (p190), two ITRs in a head-to-tail orientation (p333 and p280), and three ITRs (p345) in isolated circular intermediates. The restriction pattern of pCisAV.GFP3ori (U; uncut, P; PstI cut, S; SphI cut) and 1 kb DNA ladder (L) are also given for comparison. One additional circular form (p340) was repetitively seen and had an unidentifiable structure which lacked intact ITR sequences. Circular concatamers were identified by partial digestion with AseI for clones p280 (dimer) and p333 (monomer) as is shown in Panel B. Sequence analysis (Panel C) of six clones with identical restriction patterns to p333 (Panel A) was performed using primers (indicated by arrows) juxtaposed to the partial p5 promoter (dotted line) and ITRs (solid line) (SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and SEQ ID NO:13). The top sequence (SEQ ID NO:3) represents the proposed head-to-tail structure of intact ITR arrays with alignment of sequence derived from individual clones. The junction of the inverted ITRs is marked by inverted arrowheads (at 251bp). Several consistent bp changes (shaded) were noted in the 5' ITR D-sequence (boxed) within four clones (p79, p81, p87, and p88). All bp changes are indicated in lower case letters.

The paragraph beginning at line 1, page 16 of the specification is amended to read as follows:

Figure 11. Chemical sequence homology of three AAV circular intermediates (SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6) with various conformations of ITR arrays. Diversity in ITR arrays are evident from the non-conserved bases marked in lower case. The ends of the sequence (underlined) represent SphI restriction enzyme sites within head-to-tail circular AAV genomes cloned with the AV.GFP3ori shuttle virus.